Daily testing of contacts: adherence, number of tests, speed of tracing, and missed tests

Billy J Quilty, Stefan Flasche, W John Edmunds on behalf of the CMMID COVID-19 Working Group

This document was updated on 2nd March 2021 to include analysis on the effect of missing tests. The baseline scenario was also changed to 0 days tracing delay and 0 days LFT postage delay to reflect usage in schools and workplaces.

Summary

- Daily contact testing (DCT), i.e, the daily testing of contacts of SARS-CoV-2 infected cases with lateral flow tests (LFTs) to allow for the avoidance of quarantine if continually test-negative, has been suggested as a possible strategy to increase adherence and case-ascertainment rates while reducing onwards transmission and the burden of quarantine(1).
- We have previously shown that daily contact testing for 5 days with LFT is only 12% (95% UI: -43, 40%) less effective in averting onward transmission than a 14-day quarantine (assuming 50% adhere to quarantine and 67% adhere to self-isolation upon symptoms or a positive test)(1).
- Here we determine the effectiveness of DCT with LFTs in comparison to the current 10-day quarantine, varying: the level of adherence to either policy; the number of days of tests; the speed of contact tracing and test kit postage; and the sensitivity of LFTs.
- In a baseline scenario of tracing and testing occurring immediately after the index case receives their positive test, i.e, in a school or workplace, we find that 7 days of testing may require an approximately 20% greater increase in adherence compared to a 10-day quarantine. If adherence to DCT is found to be higher than that of a 10-day quarantine, then additional transmission may be averted.
- Increased contact tracing delays may decrease the effectiveness of DCT, but may require fewer tests (i.e, from 7 to 5) to be used as contacts may already be exiting the incubation period.
- Missed tests, i.e, over the weekend, reduces the effectiveness of shorter courses of DCT if individuals do not self-isolate in the interim, and should be minimised if possible through at-home testing or instruction to self-isolate.
- Daily contact testing without quarantine for 5+ days may reduce transmission to the same degree as that of a 10-day quarantine and may exceed if the scheme results in an increase in adherence.

Method

Using a previously published model(1) of individual viral load trajectories, we estimated the amount of transmission prevented either through daily contact testing (DCT) or a 10-day quarantine for contacts of confirmed index cases. In the model, infected individuals' natural history of infection is defined by a time of exposure, symptom onset and cessation of shedding (Figure S1, Table S1). Index cases (assumed symptomatic) become infectious once their Ct (on an inverse proportional log-scale to viral load) drops below 30 (Figure S1). The exposure times of secondary cases then occur between the start of the index case's infectious period, and their symptom onset, at which point we assume they self-isolate and seek out a PCR test, which is returned positive after 24 hours. This triggers contact tracing, which in our baseline scenario of work or school tracing takes 0 days to notify and either quarantine contacts for 10-days since last exposure, or immediately begin testing in DCT. In DCT, participants are issued 3, 5, 7 or 10 tests, with one taken daily (with 7 tests being the baseline). A negative test allows for a 24 hour period in which participants are not required to quarantine; however, any positive test will result in the participant isolating for a further 10 days. As is currently practiced in pilot studies, individuals cease daily testing if 10 days have elapsed since they were last exposed to the case. The probability of detection by lateral-flow test (LFT) is determined by the Ct at time of testing drawn from their individual viral load trajectory; the sensitivity for a given Ct is derived from fitting a logistic regression model to data from the Liverpool Community Testing pilot(2). All individuals who eventually become symptomatic (69% of individuals on average) are assumed to self-isolate at symptom onset in both strategies, whereas asymptomatic individuals do not develop symptoms and hence will not self-isolate unless they receive a positive test. Asymptomatic individuals are assumed to shed virus for 40% less time than symptomatic individuals(3,4). Adherences to quarantine and self-isolation are parameterised as being binary variables sampled for each individual, indicating either complete adherence or complete non-adherence, with the baseline being full adherence. Full model parameters are given in Table S1.

The effectiveness of each strategy (defined as ability to avert transmission potential) is then calculated as the sum of all secondary case's infectious periods spent in self-isolation or quarantine, divided by the sum of all untruncated infectious periods. For each run, we generate 1000 index cases with 10 secondary cases each - as we focus on averting this transmission rather than on the generation of additional cases through sampling from an offspring distribution, the average amount of infectivity in secondary cases averted by quarantine or testing is independent of the number of additional cases generated, and the choice of the number of secondary cases affects the width of the confidence intervals (CIs; here we consider a reasonable upper bound on secondary cases in an attempt to faithfully characterise real-world uncertainty).

Sensitivity analysis

To assess the impact of adherence, we vary the level of adherence to either policy (self-isolation upon a positive DCT LFT, or 10 days of quarantine) from 0-100%. We evaluated the effect of delays in contact tracing (time from the positive test of the index case to notification and quarantine of their

contacts) and in postage of LFTs if conducted for at-home testing, with sensitivity analysis using 1 and 2 days for tracing delays, and 2 and 4 days for postage delays. We also assess the impact of missing 1 or 2 tests, which may occur in schools or workplaces over the weekend, with individuals assumed to not self-isolate in this time as a worst-case scenario for onwards transmission. Missed tests may occur at any time in the period of daily testing, and 2 missed tests are assumed to occur consecutively.

Results

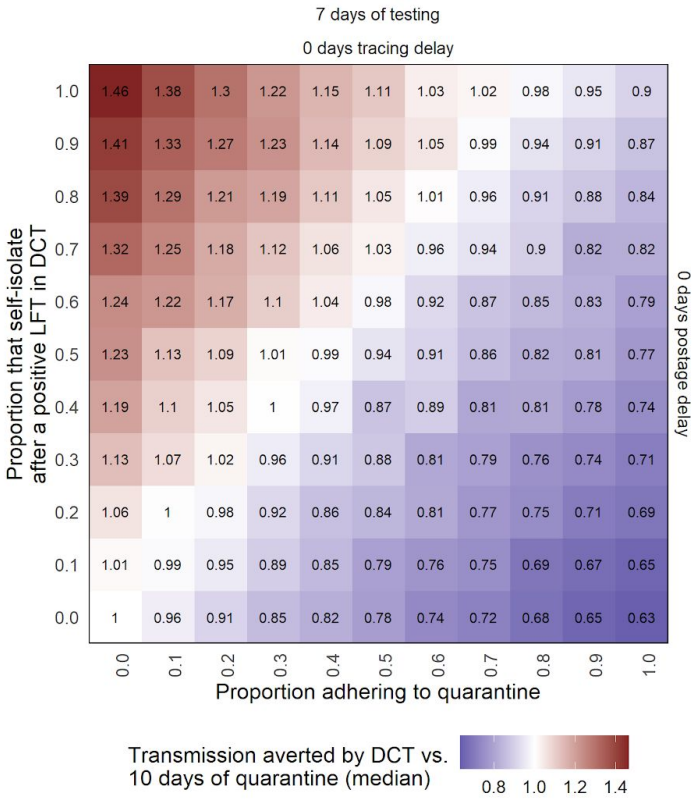

Figure 1: Relative amount of transmission potential averted by 7 days of daily contact testing (DCT) with lateral-flow tests (LFT) compared to 10 days of quarantine (current policy), varying the proportion who adhere to quarantine (x-axis) and the proportion who adhere to self-isolation following a positive test (y-axis). Values greater than 1 (red) indicate more transmission averted by DCT; values less than 1 indicate more transmission averted by quarantine.

We find that for 7 days of DCT (with 1 day from the index case's onset of symptoms, 0 days to notify contacts, and 0 days to deliver LFTs), the level of adherence required to match the median amount of transmission averted by a 10-day quarantine with the same level of adherence would need to be approximately 20% greater (Figure 1), with a greater amount of transmission averted if adherence to DCT is relatively higher than that of adherence to a 10-day quarantine. Additional days of testing do not provide much additional benefit (Figure S3).

Reducing contact tracing delays results in an increase in the amount of transmission potential averted through DCT, with shorter delays requiring a greater number of days of tests in order to avert more transmission. Increased postage delays increases the amount of transmission averted, as individuals are required to quarantine until they receive their tests and many only cease quarantining if they receive their kits and register a negative test result (Figure 2).

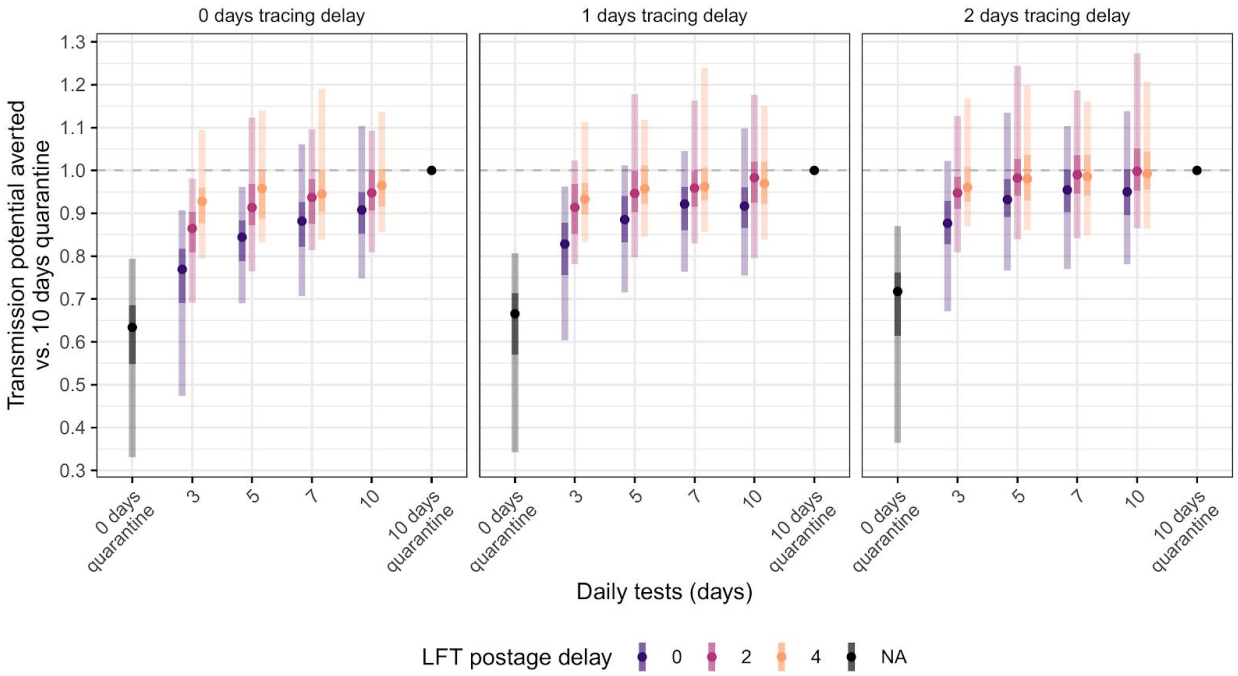

Figure 2: Relative amount of transmission potential averted by 3, 5, 7, or 10 days of daily contact testing (DCT) with lateral-flow tests (LFT) compared to 10 days of quarantine (current policy), varying the delay to receiving LFA tests and the delay to tracing of contacts after an index case's positive test. A zero day quarantine (i.e no intervention except self-isolation upon symptom onset) also shown for comparison.

Tracing and postage delays affect which of daily tests will detect an infected individual (Figure 3). Longer tracing delays cause a greater proportion of cases to be detected on the initial tests; shortening these delays increases the relative contribution of later tests. Increased postage delays also increases the relative proportion of cases detected by initial tests. While increased postage delays decrease the overall proportion of cases detected by any test, these individuals are assumed to self-isolate until they have received their kits, and as such this does not result in decreased programme effectiveness. Missed tests reduce the amount of transmission averted when compared to a 10-day quarantine, with greater losses observed with shorter tracing delays and shorter days of testing required (Figure 4).

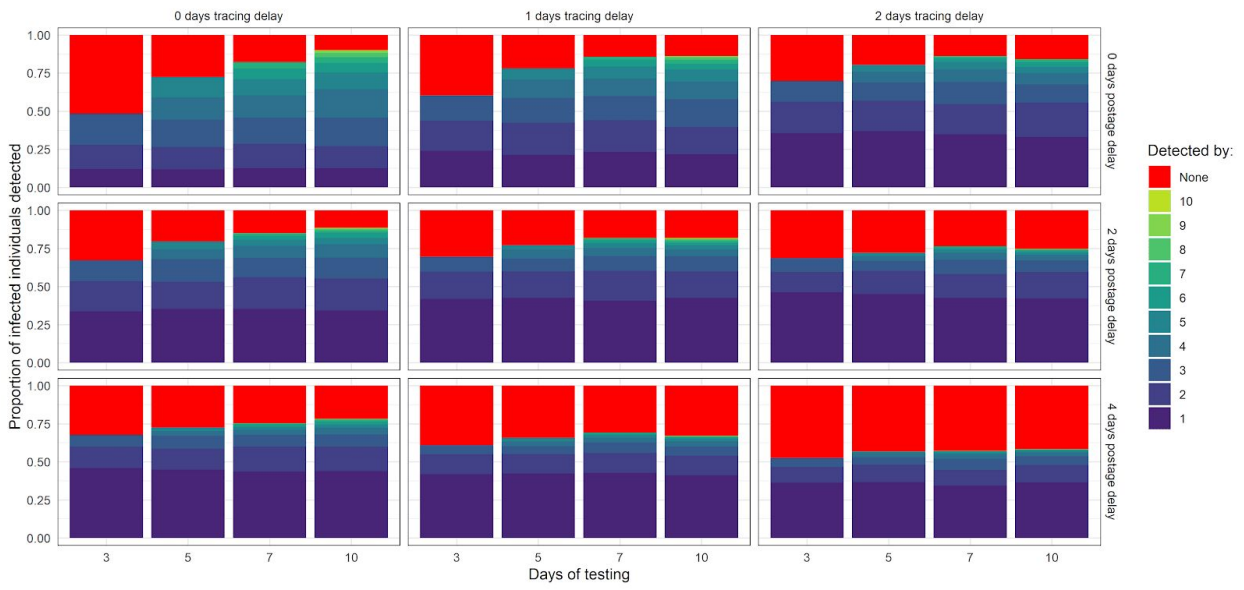

Figure 3: Proportion of infected contacts detected by each daily test, varying tracing delays (time from an index case having a positive test to the notification of contacts) and LFT postage delays (time from notification to receiving test kit). Note: those not detected due to tracing delays are assumed to be yet unaware that they have been exposed, and are hence considered infectious; those not detected due to a longer postage delay are assumed to be in isolation waiting for a test, and hence are considered not infectious.

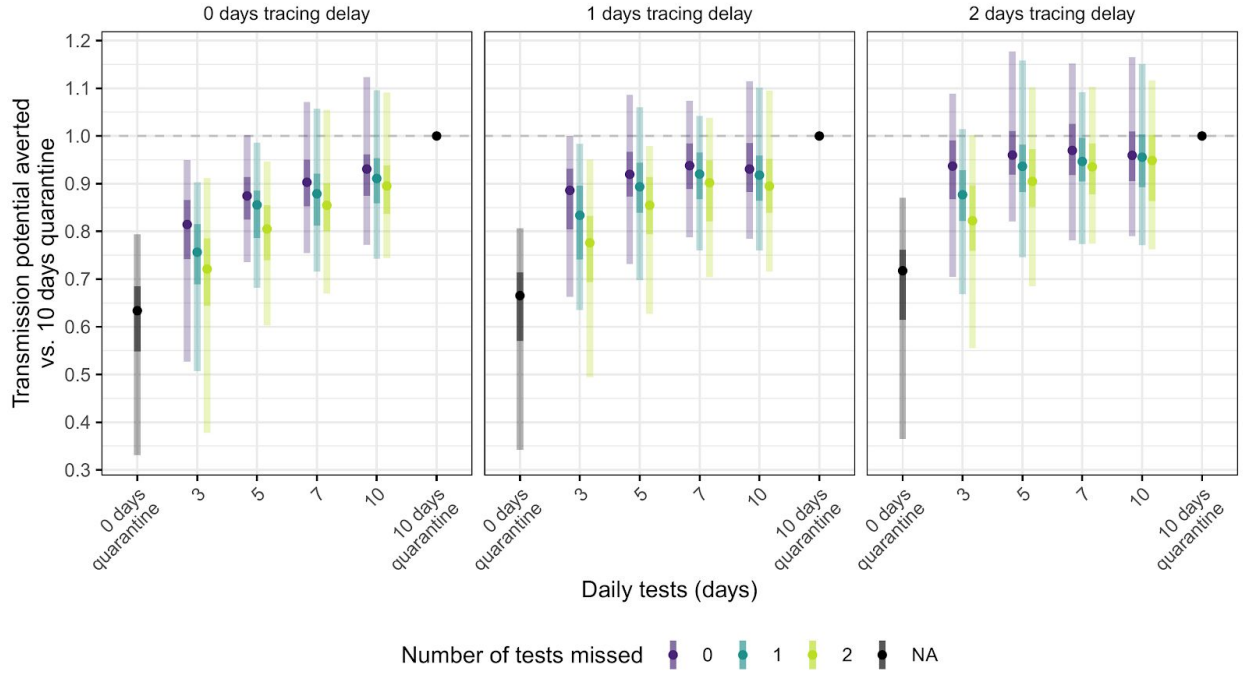

Figure 4: Relative amount of transmission potential averted by 3, 5, 7, or 10 days of daily contact testing (DCT) with lateral-flow tests (LFT) compared to 10 days of quarantine (current policy), varying the number of tests

missed and the delay to tracing of contacts after an index case's positive test. A zero day quarantine (i.e no intervention except self-isolation upon symptom onset) also shown for comparison.

Discussion

Using a model of individual SARS-CoV-2 viral load trajectories and contact tracing event timings, we find that daily contact testing for 7 days may require an approximate 20% increase in adherence to match the effectiveness of a 10-day quarantine if testing or quarantine occurs immediately after the index case returns a positive test. This indicates that if a slightly greater proportion of individuals adhere to self-isolation following a positive test in DCT than would otherwise adhere to quarantine, then additional risk of transmission introduced through possible false negatives in DCT may be counteracted. Hence, DCT could not only reduce the social and economic costs associated with contact tracing, but also reduce the epidemiological costs by reducing transmission from potentially exposed individuals.

Delays in contact tracing and delivery of LFTs in daily testing may impact the effectiveness of DCT. We estimate that with the baseline assumptions of 1 day from the index case developing symptoms to receiving a positive test and 0 days from the positive test to the notifying of the index case's contacts, that infected contacts will be notified on average 1.47 days (95% CI: 0.09, 5.07 days) after they were exposed to the index case, with some already infectious. Longer tracing delays increase the time exposed individuals spend in their infectious period prior to being notified; however, this delay is likely to reduce the effectiveness of both DCT and quarantine, although minimising this delay may result in a greater number of tests required in DCT in order to maximise the chance individuals are tested during their period of high viral load. In contrast, postage delays (the time from notification to delivery of LFTs (2 days (1.9 days (PHE)) may decrease transmission risk, as individuals should be instructed to quarantine from notification until they receive and begin taking their tests. Despite this, it may be desirable to reduce postage delays in order to release individuals from this short quarantine period (which may suffer from reduced adherence itself) if they test negative, as well as identify secondary cases as swiftly as possible to facilitate tertiary tracing. We recommend that individuals complete a full course of tests - counted from day of delivery rather than day of presumed last exposure to the index case - so as to best cover their likely period of infectiousness and account for any shortening in tracing delays. Missed tests (i.e over the weekend if conducting testing in schools or in a workplace) reduce the effectiveness of daily testing if individuals do not self-isolate in the interim, as we have conservatively assumed as a worst-case scenario. Missed tests should be avoided through the provision of at-home tests, or instruction to strictly self-isolate during this period; if this cannot be avoided, then additional days of testing after the break may counteract the loss in effectiveness.

There are several limitations to this study. Transmission potential is considered as the duration of the infectious period (Ct<30) not spent in quarantine or self-isolation, and does not scale with higher viral loads (other than the greater duration spent Ct<30) correlated with higher viral loads (Figure

S1)); this may underestimate the effect of isolating an infectious individual early on, prior to their peak infectivity. We also not not generate tertiary cases from secondary cases, instead simply reporting the truncation of their infectious period. Hence, we do not consider heterogeneity in the contact distribution of individuals, or breakdown by household vs. school/workplace/social, although it is possible that DCT results in stricter self-isolation within the home if an individual tests positive. We fit a logistic regression model to the results of the Liverpool Community Testing pilot to use as our baseline estimate for the probability of detection of the Innova LFT; there is evidence that the Ct values recorded in the evaluation may be systematically lower than other studies(5). Adherence to quarantine or self-isolation is treated as a static binary value for each individual which does not change over the course of infection; this may not accurately represent a degree of waning which may occur over the course of quarantine or DCT.

References

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Supplementary appendix

Table S1: Model specification

Parameter	**Description**	**Value**	**Source**
Incubation period	Time from exposure to onset of symptoms and peak viral load	Log-normal (log-mean: 1.63, log-SD: 0.5) Median 5.1 days, 95% UI: 2.3-11.5 days	McAloon et al.(6)
Infectious period	Time for which CT<30	Symptomatics: mean 7.56, SD: 1.54 days Asymptomatics: mean 4.32 days, SD: 1.09 days	Derived from model
Asymptomatic fraction of secondary cases	Proportion of infections that are asymptomatic	Beta (alpha 51, beta 115) Median 0·31, 95% CI 0.24–0.38	Derived from quantile matching 95% prediction interval (7)
Ct at exposure	Viral load upon exposure	40	
Peak Ct	Viral load at peak	Normal(mean: 22.3, SD: 4.2)	Kissler et al.(3)
Duration of viral shedding	Time from exposure to cessation of shedding	Symptomatics: Normal(17 days, SD: 0.94) Asymptomatics: 40% shorter	Cevik et al.(4) Kissler et al.(3)
Infectivity threshold	Approximate lower bound for viral load to facilitate infection	Ct<30	Kissler et al.(3) Singanayagam et al.(8) Lee et al.(9)
Sensitivity of the Innova lateral-test	Probability of detecting an infection given viral load in Ct	Logistic regression model fit to Liverpool Community testing pilot data. >50% detected at Ct<25. Sensitivity analysis: Shift Ct values +/- 2.5 (Figure S1)	Liverpool Community Testing pilot(2)
Time from index case's symptom onset to having a PCR test		1 day	

Time from index case's PCR test to tracing of contacts		Baseline: 0 day Sensitivity analysis: 1 days, 2 days.	
Additional time taken to receive LFTs		Baseline: 0 days Sensitivity analysis: 2 days, 4 days	
Time from exposure to being notified by contact tracers		Baseline: Median: 1.47 days (95% CI: 0.09, 5.07 days)	Derived from model
Adherence to quarantine	Proportion of individuals adhering to quarantine	Sensitivity analysis: 0-100%	Assumed
Adherence to daily contact testing (DCT)	Proportion of individuals who self-isolate after a positive LFT in DCT	Sensitivity analysis: 0-100%	Assumed
Adherence to post-symptom self-isolation	Proportion of individuals adhering to self-isolation upon developing COVID-19 symptoms	100%	Assumed

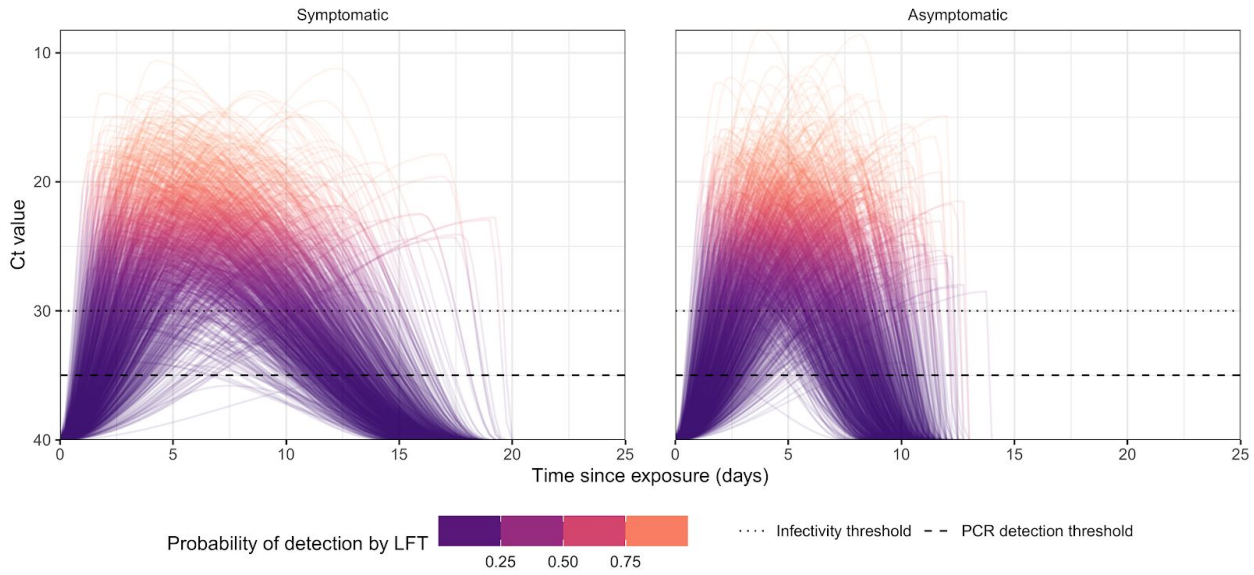

Figure S1: 1000 simulated viral load trajectories for symptomatic (left) and asymptomatic individuals (right). Probability of detection for a given Ct value derived from Liverpool Community Testing pilot. Infectivity threshold set at Ct <30(9), and PCR detection threshold at Ct<35(9).

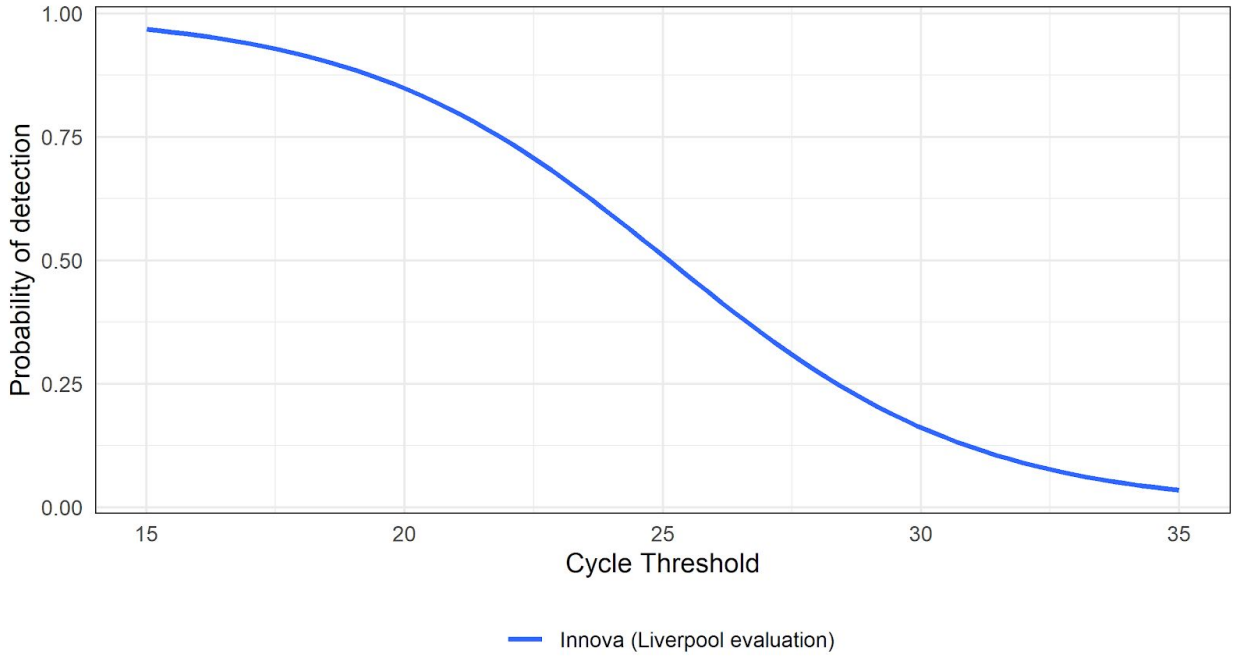

Figure S2: Assumptions for the probability of detection by lateral-flow. Logistic curves fit to Liverpool Community Testing Pilot results.

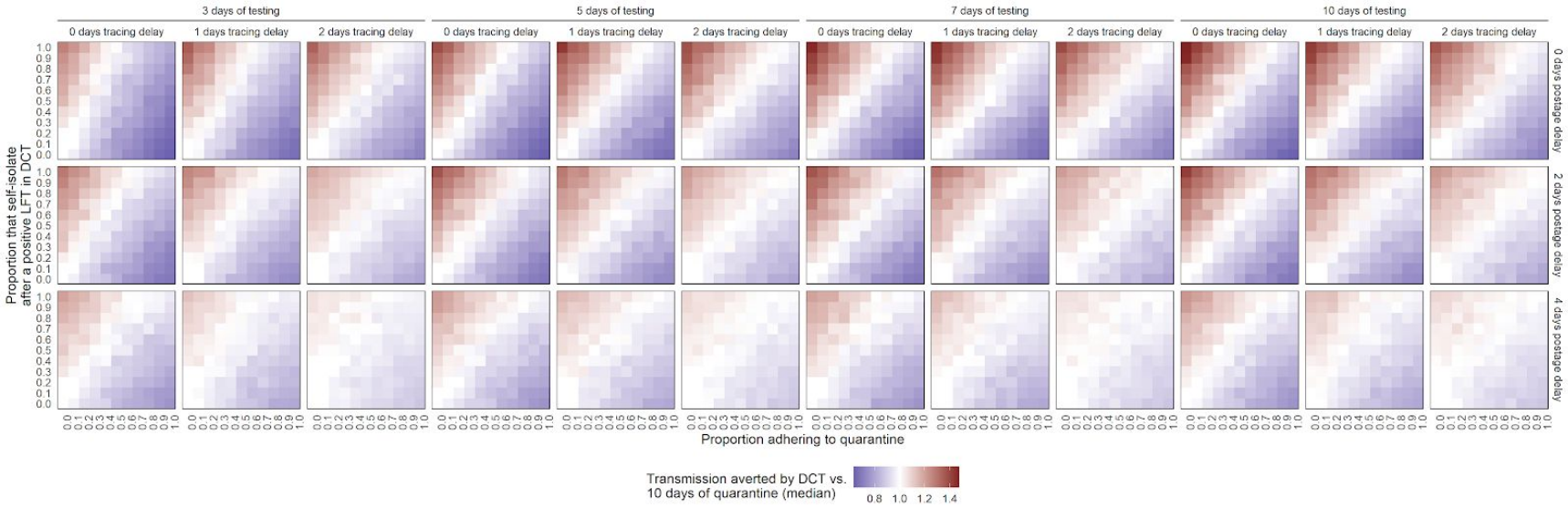

Figure S3: Relative amount of transmission potential averted by daily contact testing (DCT) with lateral-flow tests (LFT) compared to 10 days of quarantine (current policy), varying the proportion who adhere to quarantine (x-axis) and the proportion who adhere to self-isolation following a positive test (y-axis). Plot rows indicate different assumptions of postage delays, and plot columns indicate days of tests required and tracing delays. Cells in red indicate more transmission averted by DCT; cells in blue indicate more transmission averted by quarantine.